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# Solid-Solid-EC' TEMPO-Electrocatalytic Conversion of Diphenylcarbinol to Benzophenone

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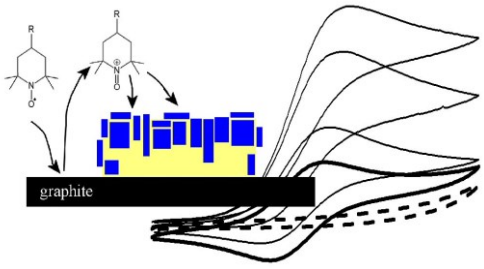
## Abstract

Voltammetry and chronoamperometry of water-insoluble microparticles is demonstrated for a mediated reaction. The solid-solid TEMPO-mediated electrolytic conversion of diphenylcarbinol to benzophenone is investigated employing 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and TEMPO derivatives (4-carboxy-TEMPO, 4-methoxy-TEMPO, 4-amino-TEMPO, 4-acetamido-TEMPO) in alkaline carbonate buffer. Chronoamperometry experiments reveal (at least) two reaction stages with (i) a high current onset (ca. 30 s) with nucleation and growth of product and (ii) a first order transport controlled reaction (ca. 5 minutes) leading to bulk conversion. It is shown that the type of TEMPO derivative as well as the pH (but not the TEMPO concentration) affects the reaction rate. The 4-acetamido-TEMPO derivative is the most effective mediator.

## Keywords

Electrocatalysis, solid state electrolytic conversion, anti-oxidant, nucleation, chrono-amperometry, organic electrosynthesis.

## Graphical Abstract



## 1. Introduction

The organic radical compound 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) is commonly used as a catalyst or mediator in organic syntheses for the chemical oxidation of primary alcohols to aldehydes, oxidation of sulphides, or conversion of organometallic compounds [1]. In 1987 Anelli et al. showed that it is possible to oxidize primary alcohols to aldehydes or carboxylic acids in the presence of sodium bicarbonate and potassium bromide using the TEMPO derivatives as the catalyst. Anelli's oxidation revealed that the transformation of aldehydes into carboxylic acids in presence of the TEMPO as the mediator can be fast [2]. TEMPO is a stable radical, which can be not only chemically but also electrochemically oxidized to the ($TEMPO^+$) oxoammonium cation in order to mediate catalytic reactions [3,4,5,6]. The mechanism of the TEMPO mediated oxidation reaction was repeatedly investigated [7,8]. The mechanism of the electrochemical oxidation of the oxoammonium cation is strongly dependent on the pH of the reaction medium. The reaction pathway under basic conditions has been suggested to be based on hydride transfer with the TEMPO oxoammonium cation converted to the corresponding hydroxylamine [9] (see Figure 1). A comproportionation of the hydroxylamine with the TEMPO oxoammonium cation is then responsible for the regeneration of the TEMPO reagent [10,11,12]. Jin et al. described a simple method for rapid voltammetric screening of TEMPO mediators for oxidation of renewable biopolymers such as cellulose. Their work was based on a range of TEMPO derivatives and revealed information about reaction rates and the stability of mediators [13]. Perhaps surprisingly, transport in the solid cellulose substrate structure played a more important role than redox driving force in the overall reaction rate.

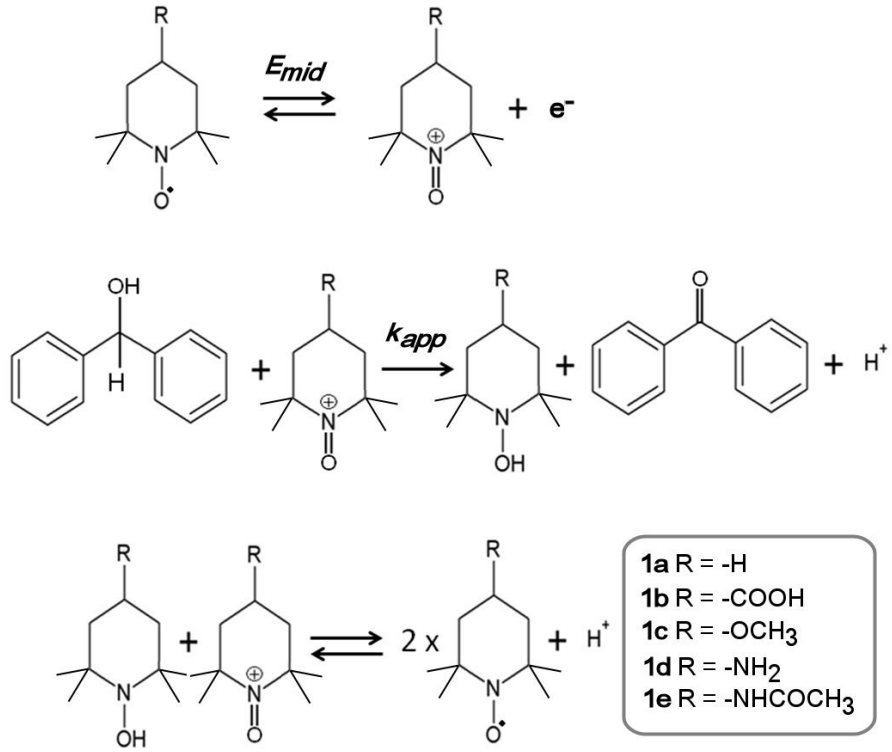



**Figure 1.** Reaction scheme (following [14]) for the TEMPO catalysed oxidation of diphenylcarbinol to benzophenone.

The main intention of the present study is to explore TEMPO mediated oxidation for the case of a solid-solid conversion of diphenylcarbinol to benzophenone, with both starting material and product water-insoluble. A range of TEMPO derivatives are investigated and a novel approach to solid state electrochemistry is introduced with the starting material and the product both *redox inactive* and immobilised at the electrode surface (compare to the voltammetry of microparticles where *redox active* materials are immobilised [15,16]). This method ensures a stable mediator

concentration and direct insight into the reaction progress for a solid-solid conversion from chronoamperometry traces.

## 2. Experimental

**2.1. Chemicals and materials.** TEMPO (97%), 4-carboxy-TEMPO (98%), 4-methoxy-TEMPO (97%), 4-amino-TEMPO (97%), 4-acetamido-TEMPO (97%), diphenylcarbinol (DPC, 98%) were purchased from Sigma Aldrich. Other chemicals such as NaOH and $NaHCO_3$ were purchased from Aldrich and used without further purification. In this study 0.1 M concentration carbonate buffer pH 11 was prepared using sodium hydroxide and sodium bicarbonate. All of solutions in this work were prepared using ultrapure water with 18.2 MΩ cm resistivity.

**2.2. Electrochemistry.** Cyclic voltammetry (CV) and chronoamperometry (CA) measurements was performed and recorded with an Autolab PGStat12 (Metrohm Autolab) electrochemical system. The electrochemical measurements were conducted using a three electrode system. The working electrode was graphite electrode (pyrocarbon, Le Carbon Lorraine) with 4.9 mm diameter mounted in a Teflon holder. A platinum wire and saturated calomel electrode (SCE, Radiometer) were used as the counter and reference electrode, respectively.

**2.3. Methodology.** Before each experiment, the graphite electrode was polished on a polishing Buehler micro-cloth and then cleaned using deionized water and acetonitrile. Next 80 nmol of diphenylcarbinol (DPC) in acetonitrile as solvent (4 μL of a 20 mM solution) were deposited onto the working electrode using a micropipete. The diphenylcarbinol solution spread evenly

over the electrode and the solvent evaporated under ambient conditions. The graphite electrode was then immersed into aqueous buffer solution of 1 mM TEMPO derivative at pH 11.

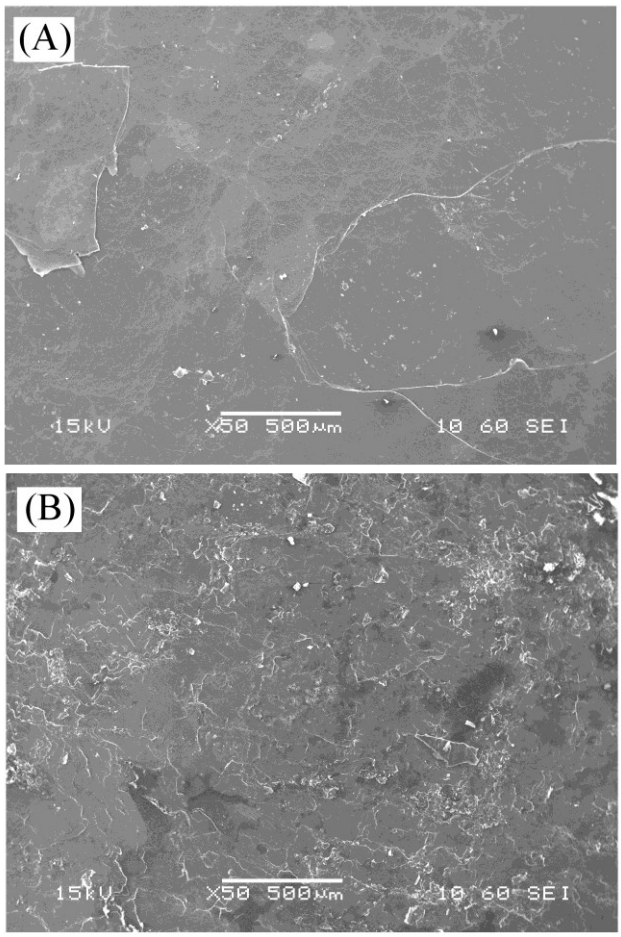



**Figure 2.** Scanning electron microscope (SEM) images for (A) 80 nmol diphenylcarbinol on graphite before TEMPO oxidation and (B) after TEMPO oxidation.

Electron micrographs of the graphite surface with diphenylcarbinol deposit (Figure 2A) reveal small amounts of material (bright patches) distributed over the surface without significantly

blocking the electrode surface. An electron micrograph obtained after oxidation of diphenylcarbinol to benzophenone (5 minute electrolysis at 0.6 V vs. SCE in 1 mM TEMPO in 0.1 M carbonate buffer pH 11; see Figure 2B) appears to show a similar distribution of material with more graphitic edge sites showing deposits. Analysis of starting material and product dissolved off the graphite surface into acetonitrile and injected into a GC-MS (Agilent 7890A GCMS with a HP-PLOT/Q, 30 m long 0.530 mm diameter column) confirms clean (ca. 99%) conversion of diphenylcarbinol to benzophenone.

## 3. Results and Discussion

### 3.1. TEMPO-Mediated Solid-Solid Oxidation of Diphenylcarbinol I.: Voltammetry

First, experiments were performed with TEMPO as electro-active compound in solution and without any diphenylcarbinol deposit at the electrode surface. The measurements were conducted in alkaline 0.1 M carbonate buffer solution at pH 11. These conditions provide a good balance between conversion and decomposition of the mediator by detrimental reaction of oxoammonium cation with hydroxide [17]. The cyclic voltammetry data for the TEMPO system indicated a stable ratio of anodic and cathodic current (see Figure 3A). Peak currents are proportional to square root of potential scan rate consistent with a diffusion controlled one-electron transfer (see inset in Figure 3A).

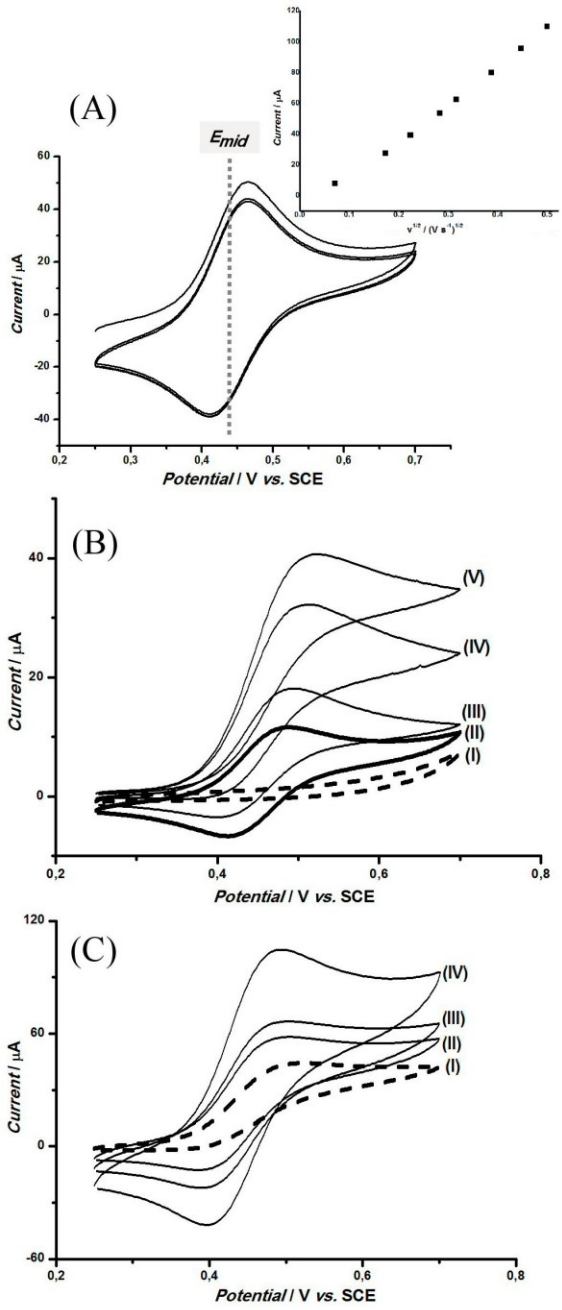



**Figure 3.** (A) Cyclic voltammograms (scan rate 0.05 $Vs^{-1}$) recorded at a 4.9 mm diameter graphite electrode for the oxidation of 1 mM TEMPO in carbonate buffer pH 11 (3 potential cycles over-layed). Inset: plot of anodic peak current *versus* square root of potential scan rate. (B) Cyclic voltammograms (scan rate 0.005 $Vs^{-1}$) for (I) DPC added in the absence of TEMPO in pH 11 carbonate buffer solution, (II) 1 mM TEMPO without DPC deposit on the graphite electrode, (III) 40 nmol DPC, (IV) 80 nmol DPC, and (V) 160 nmol DPC. (C) Cyclic voltammograms (scan rate (I) 0.005 $Vs^{-1}$, (II) 0.05 $Vs^{-1}$, (III) 0.1 $Vs^{-1}$, and (IV) 0.2 $Vs^{-1}$) for the oxidation of 1 mM TEMPO in 0.1 M carbonate buffer pH 11 with 80 nmol DPC.

The midpoint potential for TEMPO oxidation is $E_{mid}$ = ½ $E_{p,ox}$ + ½ $E_{p,red}$ = 0.44 V vs. SCE with a peak-to-peak separation of 0.07 V for a scan rate ranging from 0.005 to 0.25 $Vs^{-1}$. The experiments show that the electrochemical oxidation of TEMPO is highly reversible and mainly diffusion controlled in the absence of the diphenylcarbinol deposit (the plot in the inset in Figure 3A shows some degree of non-linearity possibly due to some adsorption of TEMPO). Figure 3B (I) shows that there is no voltammetric response for diphenylcarbinol deposited onto the graphite electrode in the absence of TEMPO in solution. Therefore there is no direct electrochemical conversion without the redox mediator. To demonstrate the impact of TEMPO mediator on the chemical oxidation of diphenylcarbinol to benzophenone, three amounts of diphenylcarbinol substrate were applied to the graphite electrode (see Figure 3B). The shape of the resulting voltammograms is consistent with a solid-solid-EC' redox process, where the oxidised TEMPO in solution reacts with the diphenylcarbinol deposit on the electrode surface (see Figure 1). This mediated reaction can result in conversion of diphenylcarbinol to benzophenone (both solid) with the reformation of the TEMPO mediator close to the electrode surface. The diffusion time from the electrode to the location of the redox conversion is very short and therefore the concentration of the oxidised redox mediator is assumed to be maintained at all times to simplify the kinetic analysis. According to the proposed mechanism, conversion of diphenylcarbinol to benzophenone consumes overall two equivalents of the TEMPO oxoammonium cation equivalent to a two-electron oxidation. The resulting catalytic current appears to be approximately proportional to the DPC amount up to 80 nmol deposit. For higher amounts of

deposit currents are lower than anticipated presumably due to onset of electrode blocking effects and noticeable concentration polarisation of the $TEMPO^{0/+}$ system.

Figure 3C shows data for 80 nmol DPC and as a function of the potential scan rate. With a scan rate of approximately 0.05 $Vs^{-1}$, the electrochemical back-reduction of $TEMPO^{+}$ can be observed, which suggests that on this time scale the chemical reaction of $TEMPO^{+}$ with diphenylcarbinol is too slow to compete. The initial rate constant $k_{app}$ can be estimated from the "transition scan rate" [18] in this case as $\frac{v_{trans} \times F}{RT} = 2\ s^{-1}$. It is likely that this value reflects the initial stages of the reaction of $TEMPO^{+}$ with diphenylcarbinol at the surface of the solid before substantial amounts of product have been formed (*vide infra*). Further and time-dependent information can be obtained from chronoamperometry experiments.

### 3.2. TEMPO-Mediated Solid-Solid Oxidation of Diphenylcarbinol II.: Chrono-amperometry

It has been shown that TEMPO derivatives can react with different rates dependent on their midpoint potential but also dependent on substrate structure. Here, a solid diphenylcarbinol substrate is converted into a solid benzophenone product and the rate of conversion is accessible directly by solid state chronoamperometry with the substrate immobilised at the electrode surface. This experimental method ensures that at a high enough applied potential a known and stable concentration of $TEMPO^{+}$ mediator is present to react with the solid substrate. The Faradaic current associated with the diphenylcarbinol conversion can be directly measured and analysed as a function of time.

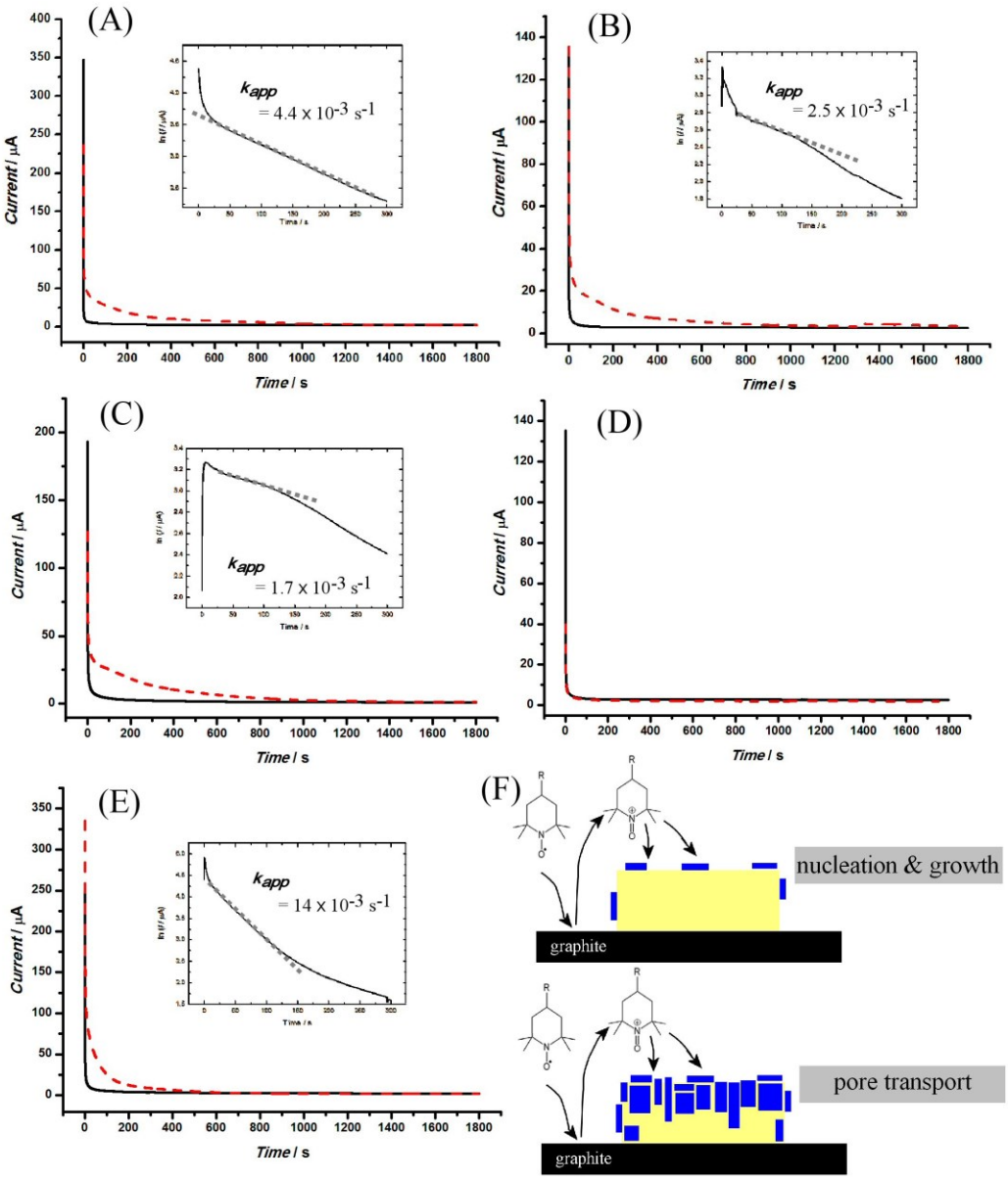



**Figure 4.** Chronoamperometry data for oxidation of 80 nmol of DPC immersed in 0.1 M carbonate buffer pH 11 and 1 mM (A) TEMPO, (B) 4-carboxy-TEMPO, (C) 4-methoxy TEMPO, (D) 4-amino-TEMPO, and (E) 4-acetamido-TEMPO. (F) Schematic plot of the initial "nucleation and growth" stage and the "pore transport" stage of the solid-solid reaction (yellow = diphenylcarbinol, blue = benzophenone).

Figure 4 shows chronoamperometry data for five different TEMPO derivatives reacting with 80 nmol diphenylcarbinol deposit on the graphite electrode. It can clearly be observed that there are differences in reaction rate for conversions of substrate to product. In the case of 4-amino-TEMPO (Figure 4D) the reaction between diphenycarbinol and $TEMPO^+$ cation is not observed at all and the chronoamperometry curves with and without diphenylcarbinol present appear identical. For all other TEMPO derivatives a clear reaction is observed usually within the first 10 minutes of the experiment. Integration of the additional Faradaic current due to mediated diphenylcarbinol oxidation suggest between 1 and 2 electrons per substrate molecule are consumed (see Table 1). The lack of full conversion (in contrast to resutls by GCMS product analysis, see Experimental) could be due to some diphenylcarbinol solid being lost from the electrode surface.

In order to investigate the progress of the reaction, a plot of the logarithm of Faradaic current (the underlying mediator current has been subtracted) versus time is revealing. Figure 4 shows that for all TEMPO derivatives there are regions of linearity where an apparent first order rate constant can be extracted. This region of linearity is usually within the first 5 minutes and after an initial onset surge in current. Rate constant data range from $1.7 \times 10^{-3}$ $s^{-1}$ for 4-methoxy-TEMPO to $14 \times 10^{-3}$ $s^{-1}$ for 4-acetamido-TEMPO, with the latter clearly being the most potent mediator in this case. When comparing to the midpoint potentials for TEMPO mediators, 4-acetamido-TEMPO clearly appears to be the mediator with the highest driving force for this

oxidation. However, this correlation is not satisfactory with 4-methoxy-TEMPO reacting surprisingly slowly. Further data from chronoamperometry are summarised in Table 1.

**Table 1.** Summary of voltammetry and chronoamperometry data for the reactivity of diphenylcarbinol microcrystals deposited onto a graphite electrode surface towards TEMPO mediated oxidation.

| **Mediator and conditions** | $E_{mid}$ **/ V *vs*. SCE** | **Number of electrons per DPC molecule** | **Reaction rate** $k_{app}$ / $s^{-1}$ |
|---|---|---|---|
| Effect of mediator structure (with 80 nmol DPC at pH 11) | | | |
| TEMPO | 0.44 | 1.3 | $4.4 \times 10^{-3}$ |
| 4-carboxy-TEMPO | 0.55 | 1.2 | $2.5 \times 10^{-3}$ |
| 4-methoxy-TEMPO | 0.59 | 1.2 | $1.7 \times 10^{-3}$ |
| 4-amino-TEMPO | 0.32 | - | n.o. |
| 4-acetamido-TEMPO | 0.61 | 1.1 | $14 \times 10^{-3}$ |
| Effect of mediator concentration (with 80 nmol DPC at pH 11) | | | |
| TEMPO (1 mM) | - | 1.3 | $4 \times 10^{-3}$ |
| TEMPO (2 mM) | - | 1.0 | $5 \times 10^{-3}$ |
| TEMPO (3 mM) | - | 1.7 | $8 \times 10^{-3}$ |
| TEMPO (4 mM) | - | 1.4 | $4 \times 10^{-3}$ |
| Effect of solution pH (with 80 nmol DPC) | | | |
| TEMPO (pH 10) | - | 1.1 | $1 \times 10^{-3}$ |
| TEMPO (pH 11) | - | 1.3 | $4 \times 10^{-3}$ |
| TEMPO (pH 12) | - | 1.4 | $16 \times 10^{-3}$ |
| TEMPO (pH 13) | - | 1.2 | $57 \times 10^{-3}$ |

### 3.3. TEMPO-Mediated Solid-Solid Oxidation of Diphenylcarbinol III.: Mechanism

The effect of the TEMPO mediator concentration was investigated (see Table 1) and although there is some variability, the trends seem insignificant even with a four-fold increase in the TEMPO concentration. This suggests that under the conditions employed here the concentration of $TEMPO^+$ does not affect the reaction rate. In contrast to this result, the effect of pH in the buffer solution is clearly observed (see Table 1). For every unit of pH increase the reaction rate is increased by a factor of approximately four. It is well known that more alkaline conditions increase the reaction rate for TEMPO systems, which is associated with the loss of protons from the substrate during oxidation.

The initial fast reaction rate (in the first seconds of the reaction) is likely to reflect the direct interaction of $TEMPO^+$ derivatives with the diphenylcarbinol crystal surface. However, the apparent rate constant $k_{app}$ associated with the first order mechanism observed during the first 5 minutes must be attributed to another rate limiting step. Figure 4F shows a schematic drawing of a mechanism where the solid benzophenone product is formed in the vicinity of the diphenylcarbinol starting material. This is likely to cause a "blocking" of the reactive surface and a switch of the rate limiting step from surface reaction controlled to transport controlled, for example with diphenylcarbinol molecules moving through "channels" towards the solid | electrolyte interface. A possibly related case of first order reaction rates (or nucleation followed by long time logarithmic growth) is characteristic for potential driven anodic oxide growth on metal surfaces such as titanium [19] and iron [20]. The fact that characteristic differences in

reaction rate are seen as a function of TEMPO derivative and solution pH can be traced back to the initial stages of the solid-solid conversion, which is likely to be associated with nucleation and growth. The data for 4-methoxy-TEMPO in Figure 4C reveal a much lower onset current, which suggests that the early stages of the reaction are slow followed by a slower than expected later stage. A plausible explanation can be based on the idea that rapid nucleation in the early stages of the reaction will yield many smaller nuclei which leaves more "channels" towards the surface during the later "transport controlled" stages of the reaction. More work will be required to confirm this hypothesis for a wider range of substrates and conditions.

## 4. Conclusion

It has been shown that the reaction of water-insoluble microcrystalline solids with redox mediators dissolved in aqueous buffer solution can be studied directly. Immobilisation of the substrate diphenylcarbinol has been demonstrated to affect the voltammetric and chronoamperometric behaviour of TEMPO derivatives consistent with the occurrence of a solid-solid EC' mechanism, where diphenylcarbinol is converted into benzophenone. The chronoamperometry method when conducted without any detrimental electrode "blocking", provides direct rate information and evidence for (i) an onset period with higher currents associated with initial nucleation and growth and (ii) a first order rate process associated with a transport-controlled reaction, presumably the transport of diphenylcarbinol into the reaction zone.

This methodology could be of wider use and beneficial in particular for the screening of anti-oxidants [21]. Insights into the reaction mechanism are of use also for the development of water-based electro-organic synthesis approaches [22] where starting material and product are solids and therefore readily separated from the electrolytic buffer solution. In future, the type of electrode employed and the range of substrates and mediators will have to be further investigated and optimised according to their application.

## References


1. Barriga S (2001) Synlett 4:561
2. Anelli PL, Biffi C, Montanari F, Quici S (1987) J Org Chem 52:2559
3. Barhdadi R, Comminges C, Doherty AP, Nedelec JY, O'Toole S, Troupel M (2007) J Appl Electrochem 37:723
4. Belgsir EM, Schafer HJ, (2001) Electrochem Commun 3:32
5. Fish JR, Swarts SG, Sevilla MD, Malinski T, (1988) J Phys Chem 92:3745
6. Manda S, Nakanishi I, Ohkubo K, Yakumaru H, Matsumoto KI, Ozawa T, Ikota N, Fukuzumi S, Anzai K, (2007) Org Biomol Chem 5:3951
7. Zhao M, Li J, Mano E, Song Z, Tschaen DM, Grabowski EJJ, Reider PJ (1999) J Org Chem 64:2564
8. De Mico A, Margarita R, Parlanti L, Vescovi A, Piancatelli G (1997) J Org Chem 62:6974
9. Rafiee M, Karimi B, Alizadeh S, (2014) ChemElectroChem 1:455
10. Bailey WF, Bobbitt JM, Wiberg KB (2007) J Org Chem 72:4504

11. Green RA, Hill-Cousin JT, Brown RCD, Pletcher D, Leach SG (2013) Electrochim Acta 113:550

12. Tromp SA, Matijosyte I, Sheldon RA, Arends IWCE, Mul G, Kreutzer MT, Moulijn JA, de Vries S (2010) ChemCatChem 2:827

13. Jin Y, Edler KJ, Marken F, Scott JL (2014) Green Chem 16:3322

14. Liaigre D, Breton T, Beigsir EM, (2005) Electrochem Commun 7:312

15. Dostal A, Meyer B, Scholz F, Schroder U, Bond AM, Marken F, Shaw SJ, (1995) J Phys Chem 99:2096

16. Bond AM, Marken F, Hill E, Compton RG, Hugel H, (1997) J Chem Soc-Perkin Trans 2:1735

17. Kishioka S, Ohsaka T, Tokuda T (2003) Electrochim Acta 48:1589

18. Scholz F, Electroanalytical Methods, Springer (2005) p. 85

19. Vanhumbeeck JF, Proost J, (2009) Corr Rev 27:117

20. Brookes H, Graham F, (1993) J Chem Soc-Faraday Trans 89:547

21. Fink MP, Macias CA, Xiao J, Tyurina YY, Jiang J, Belikova N, Delude RL, Greenberger JS, Kagan VE, Wipf P, (2007) Biochem Pharmacology 74:801

22. Francke R, Little RD, (2014) Chem Soc Rev 43:2492